PANACEA OR PLACEBO? A COMPARISON OF A BRIEF MINDFULNESS-BASED INTERVENTION AND AN ACTIVE CONTROL INTERVENTION ON NEUROGENIC INFLAMMATORY RESPONSE

An Undergraduate Research Scholars Thesis

by

MADILYNN DELANE RUTHERFORD

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ABSTRACT

Panacea or Placebo? A Comparison of a Brief Mindfulness-Based Intervention and an Active Control Intervention on Neurogenic Inflammation

Madilynn DeLane Rutherford
Department of Psychological and Brain Science
Texas A&M University

Research Advisor: Dr. Mary Meagher
Department of Psychological and Brain Sciences
Department of Institute for Neuroscience
Texas A&M University

Mindfulness-based interventions have been effective at reducing symptoms of chronic inflammatory disorders, a phenomenon proposed to be mediated by altered immune system function and inflammatory response. However, the majority of clinical trials and laboratory studies conducting mindfulness-based interventions test against poorly designed control groups. Therefore, to evaluate whether mindfulness uniquely reduces inflammatory responses above potential positive expectancy (i.e., placebo), the current study evaluated the effect of a brief mindfulness-based intervention on neurogenic inflammatory responses compared to a structurally equivalent active control intervention without mindfulness components, that too was called mindfulness, in healthy young adults (N = 30). Both groups participated in their respective 5-day interventions delivered online, and then were invited to laboratory testing. During the baseline inflammatory test, no difference in flare area or flare intensity was observed between groups (p's > .05). After practicing their respective intervention in the laboratory, both groups demonstrated significant reductions in flare area (p = .023) and flare intensity (p = .005) during the second inflammatory test, however, with no group differences in rate of change. These preliminary results suggest that mindfulness may not uniquely reduce inflammatory responses

when compared to an equivalently designed active control. Rather, these findings suggest that the expectation of improvement alone was responsible for the reduction in flare following the interventions. To further investigate the role of expectancy in mediating these effects, future studies will need to obtain baseline measures of flare before intervention training, and compare these two groups to a no treatment control condition.

ACKNOWLEDGMENTS

I have immense gratitude for my research mentor, Dr. Meagher, for her guidance, wisdom and kindness. I have gained so many valuable skills while working on her research team since the Fall of 2015. This research experience has better equipped me for the PhD program I will be entering this year, and I owe it to Dr. Meagher for believing in me and allowing me to conduct this independent research project.

I would like to thank Fenan Rassu and Hans Linsenbardt for always answering my endless questions, thoroughly explaining anything confusing, and being a shoulder to lean on and vent to when research gets stressful. They created a space in the laboratory that is friendly and comforting, while also fostering growth in research skills and knowledge. Not only have they been a great example of the researcher I hope to someday be, but they also have shown me the kind of leader and teacher I would like to be for undergraduate research assistants of my own in the future.

I would like to thank the undergraduate research assistants that helped me during this process: Dustin Zimmerman, Riley Cloud and Joelle Turner. Lastly, I would like to thank my fellow Undergraduate Research Scholar candidate, Jessica Luedke, for her support when things got stressful. It was helpful to vent and laugh with someone that is equally stressed with the same tasks.

KEY WORDS

MBSR	Mindfulness Based Stress Reduction
HEP	Health Enhancement Program
MTS	Mechanical Temporal Summation
TMS	Toronto Mindfulness Scale
FMI	Freiburg Mindfulness Scale
CESD	Center for Epidemiological Studies Depression Scale
PSS	Perceived Stress Scale
DASS	Depression Anxiety and Stress Scale

CHAPTER I

INTRODUCTION

Chronic inflammation has been shown to have many negative side effects such as cancerous tumor progression (Coussens & Werb, 2002; Shacter & Weitzman, 2002), the development and severity of asthma (Nadel, 1984; Horwitz & Busse, 1995), and metabolic disorders such as diabetes (Xu et al., 2003; Hotamisligil, 2006). For these reasons and many others, much research has been done to try to find interventions to reduce inflammation in order to alleviate pain and other negative side effects. Psychological stress has been shown to increase inflammation in people with chronic inflammatory conditions (Black, 2002; Marsland, Walsh, Lockwood, & John-Henderson, 2017), therefore stress-reduction treatments have been utilized to decrease inflammation. Mindfulness-based stress reduction (MBSR) has been shown to increase overall wellbeing and reduce stress (Grossman, 2004), and has also been shown to reduce inflammation (Rosenkranz et al., 2013) and symptoms of chronic inflammatory disorders inflammation (Reiner, Granot, Soffer, & Lipsitz, 2015; Kok, Waugh, & Frederickson, 2013).

In this study, we are also utilizing MBSR as an intervention to reduce inflammation; however, we are pairing it with an equally matched, active control that is also called mindfulness in order to evaluate whether mindfulness uniquely reduces inflammation above potential positive expectancy. The active control that we are utilizing is the Health Enhancement Program (HEP), which has been proven to be an effective active control for MBSR (MacCoon et al., 2012). This program matches MBSR on all non-specific factors such as structure and length; however, it does not include the mindfulness component. Rosenkranz and colleagues (2013) utilized MBSR

and HEP in a study assessing inflammation reduction and found that inflammation was reduced by MBSR; however, there is the possibility that this was due to the placebo effect of mindfulness and believing one is meditating. In order to assess this further, we will be utilizing the same HEP program but we told participants it is mindfulness in order to assess for placebo effects. Additionally, we will be utilizing non-experienced meditators and a shorter intervention training in the hopes of developing a more clinically accessible approach to inflammation reduction.

CHAPTER II

METHODS

All procedures in this experiment were approved by the Texas A&M Institutional Review Board. Phase one and phase two of this experiment were from a required class project. Participants were given the choice to allow data from the project to be collected for this study. Each participant signed an informed consent that allowed their data from the class project to be collected for this experiment. It was clearly stated to participants that allowing or not allowing their data from the class project to be used for this study was completely optional and would in no way affect their time in the classroom, their grades or their relationship with the professor. Phase three of the experiment was non-mandatory and participants had the choice to continue onto this phase. If they chose to participate, they signed another informed consent for this laboratory study. Again, participants were informed that their participation would not have any effect on their classroom experience.

2.1 Participants

To examine the effect of mindfulness on inflammation, we collected data from a sample of 30 Texas A&M University students from a Health Psychology classroom. There were 27 females and 3 males between the ages of 18 and 22 (M = 20.53, SD = 0.74). Participants were excluded if they were below the age of 18, if they were allergic to hot peppers or if they had a thyroid condition.

2.2 Interventions

Participants were randomly assigned into either the mindfulness condition or the active control condition. There were 15 participants in each group. Each intervention consisted of 5 days of online training through the Qualtrics Survey System. The daily trainings consisted of learning topics given in audio and written formats (see *Table 1* for intervention learning topics comparison). The lessons were followed by a 20-miniute audio recording in either a guided mindfulness meditation for MBSR or a guided visualization for HEP. The HEP intervention was a) structurally equivalent to the MBSR, b) referred to as a "mindful living" intervention to participants with the word "mindfulness" used throughout the program, and c) designed to provide information on health behaviors and to feel like an intervention, but did not provide skills training in mindfulness or mindfulness meditation. There were some aspects of the HEP training that might have induced feelings of relaxation, such as the music therapy and guided visualization training; however, they did not invoke key mindfulness elements.

Table 1. Comparison of Intervention Content Between Groups

Group	Day 1	Day 2	Day 3	Day 4	Day 5
HEP	Visualization Lesson	Music Therapy	Healthy eating and nutrition	Healthy sleeping habits	Exercise
MBSR	Foundations of Mindfulness	1. Mindfulness and stress 2. Integrating mindfulness into everyday life	1. Attitudes of Mindfulness (self-compassion, non-judgment, etc.) 2. Mindful Breathing 3. Mind wandering	1. Mind traps 2. Habitual styles of thinking 3. Negative self-talk	Accepting negative emotions during meditation

Note: Each day consisted of learning topics (listed above) given in audio and written formats, followed by a 20-minute audio-recording of a guided mindfulness meditation for MBSR and a guided visualization for HEP.

2.3 Manipulation Checks

During phase two and phase three of the experiment, participants answered "yes" or "no" to these four manipulation check questions after listening to the intervention audio recordings: "Did you listen to the full recording?", "Were you engaged in the readings/recordings?", "Did you try to actively participate?", and "Do you believe you were meditating?". The Toronto Mindfulness Scale (TMS) was also used as a manipulation check after each audio recording of the interventions. Lastly, we objectively measured whether the participants practiced for the full 20 minutes of both the guided mindfulness meditation and the guided visualization by recording the time spent on the audio page using Qualtrics.

2.4 Psychological State and Trait Measures

In each phase of the study, participants completed self-report questionnaires to assess individual differences in personality, psychological states and level of mindfulness at each phase of the study. All measures were taken on computers using the Qualtrics Survey System. In phase one and phase two, questionnaires were conducted at home. During phase three, questionnaires were conducted in the laboratory.

2.4.1 Freiburg Mindfulness Inventory

The Freiburg Mindfulness Inventory was used during each phase of the study to characterize their experience of mindfulness (Walach, Buchheld, Buttenmüller, Kleinknecht, & Schmidt, 2006). This questionnaire was given during phase one to assess the participant's baseline level of mindfulness. It was given immediately after the 5-days of training in order to assess how much mindfulness has changed since baseline. Lastly, it was given at the start of the laboratory phase

in order to assess whether their level of mindfulness changed after time passed since the intervention week. During each deliverance of the FMI, participants were instructed to answer questions such as "I am open to the experience of the present moment" according to how they've felt "during the last week".

2.4.2 Toronto Mindfulness Scale

The Toronto Mindfulness Scale (TMS) was used as a manipulation check after each 20-minute audio. This scale asks participants to reflect on their experience of the meditation session immediately after it ends (Lau et al., 2006). The 13-item scale produces two subscales: curiosity and decentering. The Curiosity subscale was measured with questions such as "I was curious to see what my mind was up to from moment to moment" and the Decentering subscale was measured with questions such as "I experienced myself as separate from my changing thoughts and feelings".

2.4.3 Center for Epidemiologic Studies Depression Scale

The Center for Epidemiologic Studies Depression Scale was used during each phase of the study to measure depressive symptomatology (Radloff, 1977). Participants were instructed to respond to each item, such as "I did not feel like eating; my appetite was poor", according to how they felt during the past week.

2.4.4 Perceived Stress Scale

The Perceived Stress Scale was used during each phase of the study to measure the degree to which situations in one's life are appraised as stressful (Cohen, Kamarck, & Mermelstein, 1983).

Participants were instructed to respond to each item, such as “how often have you felt that you were on top of things?”, according to what their feelings and thoughts were like during the past week.

2.4.5 Depression Anxiety Stress Scale

The Depression Anxiety Stress Scale (DASS) was used during each phase of the study to assess for the three traits of depression, anxiety and stress (Henry & Crawford, 2005). Participants were instructed to respond to each item, such as “I felt it difficult to relax”, according to how much it applied to them over the past week.

2.5 Pain Ratings

During phase three, participants rated their pain unpleasantness and pain intensity scores using a numerical rating scale from 0-100. For intensity, 0 indicated “no pain” and 100 indicated “most pain imaginable”. For unpleasantness, 0 indicated “no unpleasant sensation” and 100 indicated “most unpleasant sensation imaginable”. During the capsaicin task, participants rated their pain intensity and pain unpleasantness through Qualtrics Survey System in 2-minute intervals during the 30 minutes that the capsaicin was on their forearm. During the MTS task, participants verbally rated their pain intensity after one stimulus and then verbally rated their peak pain intensity after a series of 10 stimuli.

2.6 Inflammation

During phase three,the inflammatory response to a topical capsaicin cream was assessed pre-intervention and post-intervention. We used 0.3 mL of Zostrix cream applied to the volar

forearms to induce the inflammation reaction on the skin. Zostrix contains 0.1% of capsaicin, an active component of chili peppers. This capsaicin-induced flare response provided a measure of local neurogenic inflammation and was used to assess if the mindfulness intervention could decrease the area and intensity of the inflammatory response, as well as the sensory and affective dimensions of the pain experience. The inflammatory "flare" response results in an area of redness, which is linked to increased blood flow to the skin, that has spread beyond the area where capsaicin cream was applied. Flare images were captured with the Laser Doppler Imaging System (MoorLD2-IR, Moor Instruments Inc., UK).

2.7 Mechanical Temporal Summation

During phase three, participants underwent a mechanical temporal summation (MTS) assessment. MTS refers to the progressive increase in pain ratings in response to a series of constant-intensity, painful mechanical stimulations (Price, 1972; Bulls et al., 2017) which is believed to result from a temporary hyperexcitability of central spinal cord neurons (Mendell & Wall, 1965) and is thought to be an indicator of central sensitization and chronic pain risk (Li, Simone & Larson, 1999). MTS was utilized to test whether mindfulness training could uniquely reduce pain facilitation as indexed by decreases in summation. This procedure utilized von Frey filaments, a set of filaments made from nylon hairs, that are designed to deliver the same, specific force each time it is pressed into the skin at a right angle. For this procedure, we utilized a 180g filament and a 300g filament. The testing sites were the dorsal surface of the hand between the thumb and index finger, the middle phalanx of the middle finger and the upper trapezius. Participants verbally gave their pain intensity scores after the first contact with the

filament and then gave a peak pain intensity rating after 10 consecutive contacts with the filament.

2.8 Data Analysis

The data was analyzed using SPSS Statistics software Version 22 (IBM, Chicago, IL, USA). Mixed ANOVAs were used to determine whether MBSR and HEP interventions differentially altered the responses to questionnaires, pain ratings and flare intensity and flare area between groups as well as changes over time. A chi-square test of independence was used for the four manipulation check questions.

2.8.1 Flare Area and Flare Intensity Analysis

Flare area and intensity scores were calculated using the Moor LDI Laser Doppler Imager Research Version 5.3 software package. The scores were calculated by a researcher that was blind to the intervention conditions. The polygon tool function was used to draw around the digitized flare image. This first drawing was done to find any white space located within the initial flare outline. The white space cannot be rated by the software due to the perfusion, which is the amount of blood flow, being too intense. We made sure to make our drawing much bigger than the flare to ensure that we included all of the regions showing increased blood flow before cutting unaffected areas. The flare area was qualified by first finding the threshold of the subject's forearm perfusion. The threshold is the average perfusion units plus two standard deviations. Once this threshold was found, we were able to cut out all areas with perfusion below this level. Everything left was deemed part of the flare. The area was then measured again using the polygon tool. This gave us the area and intensity of the flare for each participant. Next, we

used an excel sheet with formulas built in to allow us to extract the area of the flare, the mean intensity of the flare, and any white space that the software couldn't place a rating on but was part of the flare.

2.8.2 Mechanical Temporal Summation Data Analysis

One participant was excluded from data analysis because they reported that they were not making valid ratings for the pre-intervention MTS tests. In total, data from 29 participants was used in the analyses with 15 participants in the MBSR group and 14 in the active control group. In order to evaluate whether temporal summation occurred at each site, paired sample t-test were used to calculate the pain ratings from the first contact with the filament to the peak pain rating after 10 contacts with the filament. The magnitude of temporal summation (i.e., the difference scores for temporal summation at the finger, hand, and trapezius) was calculated by subtracting the pain intensity ratings following the first contact from the peak pain intensity ratings.

2.9 Procedures

2.9.1 Phase One

Informed consents were obtained by students that were willing to allow their classroom project data from phase one and phase two to be collected for this experiment. Participants then answered baseline questionnaires (DASS, CESD, PSS and FMI) and demographics questions.

2.9.2 Phase Two

Phase two occurred the week after phase one. Participants were randomly assigned into either the MBSR group or the active control group. Both groups were told that they would be doing a 5-

day online mindfulness training. Participants were sent daily links by email to the online training delivered by Qualtrics Survey System. Each day consisted of learning modules given in audio and written format followed by a 20-minute audio recording of either a guided mindfulness meditation for the MBSR group or a guided visualization for the HEP group (see *Table 1* for specific differences between the interventions). Participants answered the four manipulation check questions and filled out the TMS after each audio recording. At the end of the final day of training, participants answered the DASS, CESD, PSS and FMI.

2.9.3 Phase Three

Phase three started one week after phase two ended and it occurred over the span of three weeks. Upon completion of the 5-day intervention training, participants were invited to participate in the laboratory half of the study. Participants were given $17/per hour for their participation in this portion. When participants arrived at the laboratory, they were instructed to wash their hands up to their elbows and take off their jewelry. They were then led to another room where they were given the informed consent document and told to ask any questions they have after reading the document thoroughly. If they agreed to participate, they signed and dated the document. They were then given a series of questionnaires on a computer using Qualtrics while the experimenter left the room to allow them privacy. Upon completion of the questionnaires, the experimenter re-entered the room to conduct a pain rating training. This consisted of explaining how to use the numerical rating scales, followed by multiple practice rounds to get the participant familiar and acquainted with the ratings.

The MTS and capsaicin tests were counterbalanced so that half of the participants received the MTS test first, and half received the capsaicin test first. In the MTS task, trial location order (hand, finger and shoulder) was randomized. Each site was first probed with the 180g von Frey filament one time and a participant then gave a verbal pain intensity score. They were then probed 10 times in a row and they verbally gave a peak pain intensity score. This was then repeated with the 300g von Frey Filament before moving to the next body location.
The capsaicin task started with tracing a circle onto the participant's volar forearm. The experimenter then applied 0.3 mL of capsaicin cream inside the circle and covered it with a Tegaderm bandage to prevent evaporation (Rosenkranz et al., 2013). The participant was instructed to keep the arm with the cream completely still and to not touch the area near the cream. They were also told to make pain intensity and pain unpleasantness ratings every time they appeared on the screen in front of them in 2-minute intervals. The experimenter left the room and returned after 30 minutes. They then led the participant to another room, took of their bandage and removed the remaining cream with a cotton ball. The experimenter then took an image of the participants arm with a Laser Doppler Imaging System (MoorLD2-IR, Moor Instruments Inc., UK), a machine that measures blood flow to the surface of the skin.

After completing the MTS and capsaicin tasks, the participant was primed with their intervention by listening to the same 20-minute audio recording that they listened to during phase two. They then answered the four manipulation check questions and the TMS. After the intervention priming, the experimental procedures for MTS and capsaicin were repeated with the arms switched (i.e. if during the first-round MTS was done on the right arm and capsaicin was done on the left arm, this would now be reversed). Participants were also instructed to utilize their

intervention during these tasks. The mindfulness group was told, "Now that you have learned new mindfulness skills in the classroom, we would like you to utilize these skills during the next pain test. Feel free to incorporate concepts such as non-reactivity and non-judgment into the following pain experience, to the intense or unpleasant sensations you may feel. Also, feel free to use your breath as an anchor to the present moment while you are doing the activity". The active control group was told, "Now that you have learned new mindfulness skills in the classroom, we would like you to utilize these skills during this next pain test. Feel free to incorporate whatever concepts were most helpful for you into the following pain experience". These exact words were told to the participants before each task.

After the second round of MTS and capsaicin was complete, participants answered exit questionnaires, were debriefed and were paid $17/hour that they spent in the laboratory.

An illustration of the three phases of experimental procedures can be found in *Figure 1*.

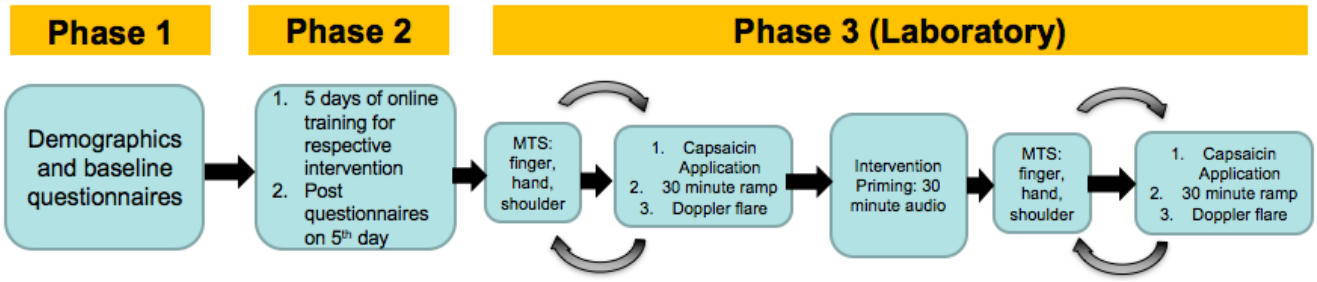


Figure 1: Procedures outline

CHAPTER III

RESULTS

3.1 Psychological State and Trait Measures

Results of repeated measures ANOVA indicated that both the mindfulness and active control group experienced significant decreases in self-reported depressive and stress symptoms, as well as increases in mindfulness (see *Table 2*).

Table 2. Comparisons of Psychological Outcomes Between Groups Across the Study

	Phase 1		Phase 2		Phase 3	
	Mean (SD)		Mean (SD)		Mean (SD)	
	HEP	MBSR	HEP	MBSR	HEP	MBSR
Freiburg Mindfulness Inventory	34.13 (5.91)$_{A}$	35.73 (7.60)$_{A}$	38.33 (7.30)$_{B}$	38.47 (4.81)$_{B}$	36.47 (4.94)$_{AB}$	36.73 (6.20)$_{AB}$
Perceived Stress Scale	22.40 (5.67)$_{A}$	19.27 (6.51)$_{A}$	15.07 (7.50)$_{B}$	16.13 (7.50)$_{B}$	15.93 (8.13)$_{B}$	14.53 (6.52)$_{B}$
Center for Epidemiologic Studies Depression Scale	20.67 (10.25)$_{A}$	20.33 (11.10)$_{A}$	13.60 (7.91)$_{B}$	14.00 (6.08)$_{B}$	12.60 (5.74)$_{B}$	15.67 (6.64)$_{B}$
DASS – Depression (Ln)	1.51 (0.73)$_{A}$	1.48 (0.84)$_{A}$	0.87 (0.77)$_{AB}$	1.27 (0.76)$_{AB}$	0.95 (0.47)$_{B}$	1.21 (0.67)$_{B}$
DASS - Anxiety	4.20 (3.17)$_{A}$	5.33 (3.77)$_{A}$	3.07 (2.15)$_{A}$	4.00 (1.51)$_{A}$	2.27 (1.67)$_{A}$	5.20 (3.73)$_{A}$
DASS - Stress	7.53 (4.00)$_{A}$	7.00 (4.36)$_{A}$	4.47 (4.27)$_{A}$	5.60 (2.44)$_{A}$	5.53 (3.42)$_{A}$	7.00 (3.70)$_{A}$

Note: Means in the same row that do not share the same subscript differ at $p < .05$. For example, subscripts "A" and "AB" do not differ, but subscripts "A" and "B" do differ.

3.2 Manipulation Checks

The data from the four manipulation check questions were analyzed using Chi Square tests. The independent variable was group and the dependent variable was the answer to each question. The TMS was also used as a manipulation check because it asks participants to reflect on what they "just experienced" immediately following the intervention recordings.

3.2.1 Phase Two

During the final day of phase two, 100% of participants in each group answered "yes" to the questions "Did you listen to the full recording?" and "Did you try to actively participate?". One participant in the mindfulness group answered "no" to the question "Were you engaged in the readings/recordings?" and 100% of participants in the control group said "yes"; however, this was not a statistically significant difference, X^2 (1, N = 30) = 0.97, p =.325. For the question "Did you believe you were meditating?", 6 participants from the mindfulness group and 5 participants from the control group answered "no". This difference was not statistically significant, X^2 (1, N = 30) = 0.14, p =.705.

TMI mixed ANOVAs revealed a significant main effect of time from Phase two, Day 1 to Phase two, Day 5 with curiosity ratings decreasing over time, F(1,28) = 4.549, p =.042, and decentering ratings increasing over time, F(1,28) = 4.779, p =.037. There was not a significant difference between groups.

3.2.2 Phase Three

During Phase three of the experiment, 100% of participants in each group answered "yes" to the question "Were you engaged in the readings/recordings?". For the question "Did you listen to the full audio?", one participant in the mindfulness group answered "no" and 100% of the control participants said "yes"; however, this difference was not statistically significant, X^2 (1, N = 30) = 1.03, p =.309. For the question "Did you try to actively participate?", one participant in the control group said "no" and 100% of the mindfulness participants said "yes"; again, this was not a statistically significant difference, X^2 (1, N = 30) = 1.03, p =.309. For the final question "Did

you believe you were meditating?", 3 participants in the control group answered "no" and 100% of the participants in the mindfulness group answered "yes"; this difference was not statistically significant, X^2 (1, N = 30) = 3.33, p =.068.

TMI mixed ANOVA results from Phase two, Day 5 to Phase three revealed that there was not a significant change in curiosity ratings, $F(1,28) = 0.494$, $p > .05$. However, there was a significant main effect of time for decentering, $F(1,28) = 13.342$, $p < .001$, with scores increasing over time.

3.3 Inflammation

3.3.1 Pain Ratings

Figures 2-5 depicts the changes in raw pain intensity and pain unpleasantness ratings over the 30 minutes that capsaicin was on the participant's arm, with ratings occurring in 2-minute intervals. The areas under the curves (AUC) were found with the pain intensity and unpleasantness data and used for the statistical analysis. For pain intensity, mixed ANOVAs of the AUCs revealed that ratings significantly decreased from the pre-intervention capsaicin ramp to the post-intervention capsaicin ramp, $F(1, 26) = 11.034$, $p = .003$; however, there was not a significant difference between groups. For pain unpleasantness, mixed ANOVAs of the AUCs also revealed a significant decrease from the pre-intervention capsaicin ramp to the post-intervention capsaicin ramp, $F(1,26) = 16.537$, $p < .001$, and a significant interaction between trial and intervention, $F(1, 26) = 4.923$, $p = .035$. *Figure 4* indicates that the change is due to the pre-intervention trial having a significant difference between groups. To further interpret this interaction between trial and condition, an independent sample t-test was used to compare groups scores on the pre-intervention unpleasantness ratings. The results indicated that the mindfulness group (M = 30.11,

SD = 24.55) had significantly lower scores than the control group (*M* = 79.36, *SD* = 84.10); *t*(26) = -2.103, *p* = .045. Taken together, the results suggest that the mindfulness training during phase two reduced pain unpleasantness ratings during the pre-intervention. However, this difference is not observed after the intervention when both groups show a significant reduction in pain intensity and unpleasantness ratings.

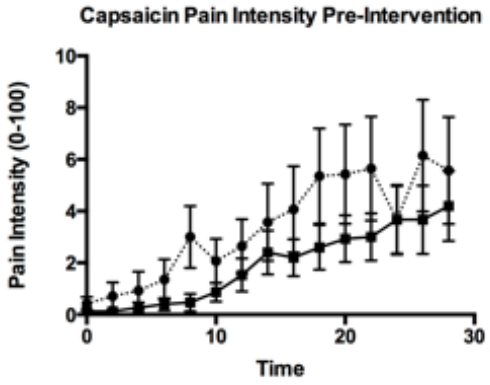
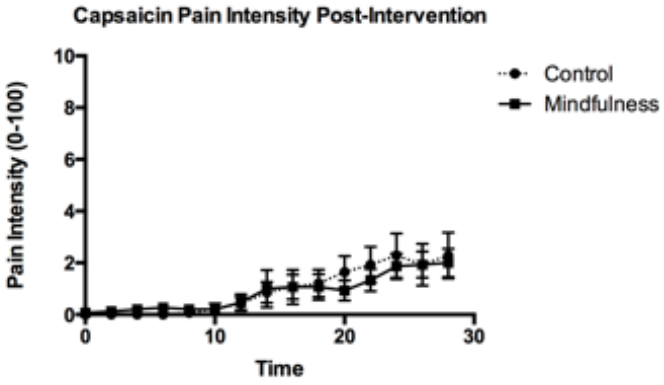


Figure 2



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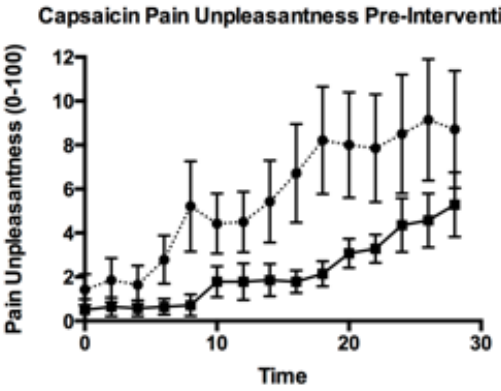


Figure 4

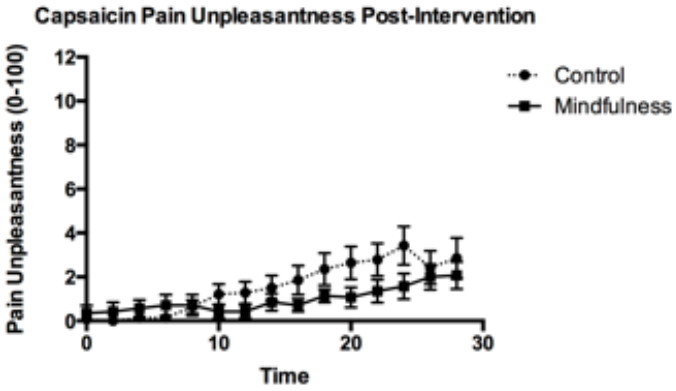


Figure 5

Figure 2-5: Mixed ANOVAs indicated a significant main effect of time for pain intensity ($p < .001$) and pain unpleasantness ($p < .001$). There was also a significant interaction between time

and group for pain unpleasantness (p = .035); however, there were no significant differences found between groups for pain intensity. Mean ± SEM.

3.3.2 Flare

Figures 6 and 7 depict the changes in flare area and flare intensity from the pre-intervention flare to the post-intervention flare. Values were long transformed to satisfy normality. Mixed ANOVAs revealed a significant main effect of time for flare area, $F(1,28) = 5.809$, $p = .023$, and flare intensity $F(1, 28) = 9.453$, $p = .005$. There was not a significant difference between groups.

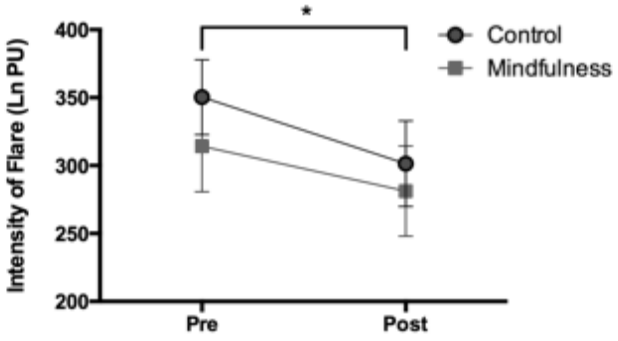


Figure 6

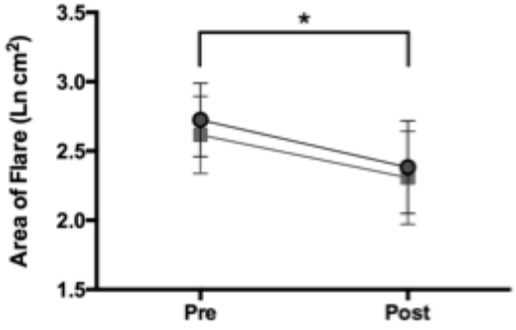


Figure 7

Figures 6 and 7: Mixed ANOVAs indicated a significant main effect of time for flare intensity (p = .005) and flare area (p = .023). No significant difference was found between groups (p > .05). Mean ± SEM.

3.4 Mechanical Temporal Summation

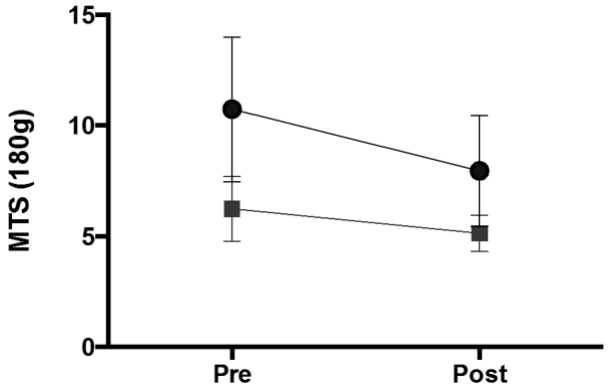
3.4.1 Manipulation Check – Temporal Summation

In order to evaluate whether temporal summation occurred at each site, paired sample t-tests were used to calculate the pain ratings from the first contact with the filament to the peak pain

rating after 10 contacts with the filament. For the pre-intervention and post-intervention 180g MTS test, paired sample t-tests revealed a significant decrease in pain ratings from first contact to peak pain rating after 10 contacts for the hand, finger, and trapezius for both intervention groups (all *p's* < .05). For the pre-intervention and post-intervention 300g MTS test, paired sample t-tests also revealed a significant decrease in pain ratings from first contact to peak pain rating after 10 contacts for the hand, finger, and trapezius for both intervention groups (all *p's* < .05). These results indicate that MTS occurred at hand, finger, and trapezius for both intervention groups at baseline and after the intervention for both 180g of pressure and 300g.

3.4.2 Mechanical Temporal Summation Pain Ratings

Pain ratings were averaged across each anatomical location. Mixed ANOVAs revealed no significant differences between groups at baseline comparisons nor post-intervention comparisons (all *p's* > .05), which can be seen in *Figures 8 and 9*.



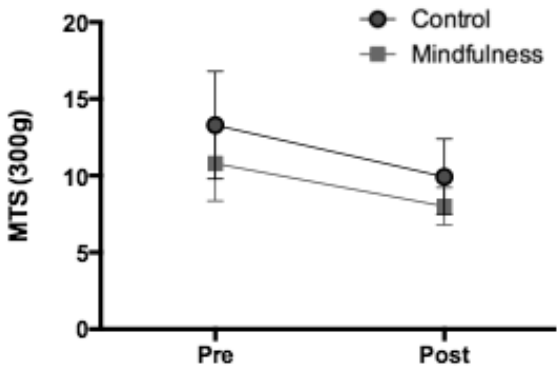


Figure 8 ***Figure 9***

Figures 8 and 9: MTS Pain Intensity Ratings for 180g and 300g filaments. Although mechanical temporal summation appears to decrease over time in the 300 mg test, mixed ANOVAs indicated no significant time nor group differences (all *p's* > .05). Mean ± SEM.

CHAPTER IV

DISCUSSION

The current study examined the psychological and neurogenic inflammatory effects of mindfulness-based stress reduction therapy and an equivalently designed active control also referred to as “mindful living”, in order to assess possible placebo effects. The results indicate that a placebo effect likely occurred due to the lack of between group differences following the interventions. Both the mindfulness and active control group experienced significant decreases in self-reported depressive and stress symptoms, as well as increases in mindfulness. The increase in mindfulness in the active control as well as the manipulation check questions in which participants indicated that they believed they were meditating is evidence for a placebo effect of being told that one is receiving mindfulness training. Participants also had significant decreases in capsaicin-induced flare intensity, flare area, and self-reported pain intensity scores from pre-intervention to post-intervention, with no significant differences found between groups at either time point.

The current study found no significant differences in changes in MTS ratings from pre-intervention to post-intervention, as well as no significant differences between groups at either time point. These results indicate that the interventions may not affect measures of central sensitization of pain in the same way they affected other measures of pain. However, it is importance to note that these statistically non-significant results might be due to the relatively small group sizes used in the study, meaning that we may be statistically underpowered to

examine the effects of MBSR viruses HEP on MTS testing, which will be discussed further in the limitations.

It is also interesting to note that the current study did observe one significant difference between groups on the capsaicin-induced pain unpleasantness scores. Results indicate that scores significantly differed between the mindfulness and control groups during the pre-intervention trial with the mindfulness group having significantly lower scores than the control group. During this pre-intervention testing, we were able to observe the long-lasting effects of MBSR training before the participants were primed with the interventions compared to the active control. Therefore, these results suggest that the MBSR group acquired the mindfulness training skill during the 5-days of MBSR training and generalized this skill to the pre-intervention pain test. In contrast, the active control group did not, and reported higher pain unpleasantness ratings. This difference between groups indicates that MBSR participants might be more capable of reducing their struggle and increasing their acceptance of pain, whereas the placebo effect of mindfulness-expectancy might not be strong enough to affect the emotional experience of physical pain in this way.

There are several limitations to this study. First, the sample size might have been too small to pull out several potential effects. For example, the results appear to be trending in the direction of having a significant main effect of time for MTS as well as an effect of MBSR training during the pre-intervention test for capsaicin-pain intensity, MTS and flare. Thus, a larger sample size could increase the power of the analyses for detecting possible significant changes such as these. Future studies should also obtain baseline measures of flare, capsaicin pain, and MTS before any

intervention training takes place in order to fully analyze the effects of the interventions. Another limitation of the study was the 5-days of intervention taking place online at home, because it is unknown whether the participants fully engaged. Future studies might have participants complete the 5-days of intervention training in a laboratory setting where their participation and engagement can be directly observed. Lastly, in order to further asses for possible placebo affects, an additional HEP group will need to be run with participants that are not told that it is a "mindful living" intervention. This may lead to an improved understanding of the role of expectancy driven changes in inflammatory symptoms for individuals experiencing chronic inflammatory disorders. This additional control group should include a relaxation effect, because there is the possibility that simply relaxing during the intervention lowered participant's sympathetic arousal and this alone lead to changes.

Nonetheless, the results of this study indicate that placebo effects related to the positive expectations of mindfulness conveyed and presumed during the interventions may have contributed to changes in mood, as well as pain experiences in neurogenic inflammatory response. Future mindfulness studies should utilize manipulation checks to analyze the possibility of a placebo affect taking place. This way, researchers can rule out placebo effects and solely analyze the true effects of internalized traits from mindfulness practice.

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